Clinical trial results:
Phase 2 Open Label Single Arm Repeat Dose Study to Assess the Effect of SNF472 on Wound Healing in Uraemic Calciphylaxis Patients

Summary

EudraCT number	2015-004313-25
Trial protocol	ES GB
Global end of trial date	14 November 2017

Results information

Result version number	v1 (current)
This version publication date	24 May 2019
First version publication date	24 May 2019

Trial information

Trial identification

Sponsor protocol code	SNFCT2015_04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02790073
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Laboratoris Sanifit
Sponsor organisation address	Parc Bit, Europa Building, Ctra. Valldemossa km 7.4, Palma de Mallorca, Spain, 07121
Public contact	R&D Department, Laboratoris Sanifit, +34 971439925, ana-zeralda.canals@sanifit.com
Scientific contact	R&D Department, Laboratoris Sanifit, +34 971439925, ana-zeralda.canals@sanifit.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 November 2017
Global end of trial reached?	Yes
Global end of trial date	14 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to evaluate the effect of SNF472 on top of standard of care on promoting wound healing and other parameters of therapeutic response in hemodialysis (HD) patients with calciphylaxis (calcific uremic arteriolopathy [CUA]).

Protection of trial subjects:

Written informed consent was obtained from each subject prior to evaluations being performed for eligibility. Subjects were given adequate time to review the information in the informed consent and were allowed to ask, and have answered, questions concerning all portions of the conduct of the study. Through the informed consent process each subject was made aware of the purpose of the study, the procedures, the benefits and risks of the study, the discomforts and the precautions taken. Any side effects or other health issues occurring during the study were followed up by the study doctor. Subjects were able to stop taking part in the study at any time without giving any reason.

Background therapy:

Standard of care for CUA was in accordance with each site’s standard procedures.

Evidence for comparator: -

Actual start date of recruitment	01 January 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	14
EEA total number of subjects	2

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	8
From 65 to 84 years	5
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

For this study, both non-hospitalised and hospitalised calciphylaxis patients were recruited after obtaining written informed consent, with a preference for non-hospitalised patients, wherever possible.

Pre-assignment

Screening details:

Potential patients for the inclusion in the clinical trial attended the Screening Visit within 14 days before receiving the first dose of IMP.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	SNF472

Arm description:

SNF472 30mg/ml or 90 mg/ml solution for infusion

Arm type	Experimental
Investigational medicinal product name	SNF472
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

SNF472, was provided as 10 or 5 mL of sterile liquid in transparent glass vials, containing either 300 mg or 450 mg of SNF472, respectively, for a concentration of 30 mg/mL or 90 mg/mL. The SNF472 solution was diluted in a 100-mL saline bag prior to administration. SNF472 was administered TIW to the subject by slow infusion (2.5 to 4 hours) during the subject's regular HD session. The dose of SNF472 administered at each session was 400 to 900 mg, depending on the subject's body weight category at screening, resulting in per kilogram doses ranging from 5.6 to 8.6 mg/kg.

Number of subjects in period 1	SNF472
Started	14
Completed	11
Not completed	3
Ceased haemodialysis and was discontinued	1
Consent withdrawn by subject	1
Death	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description:	
Intention to treat	

Reporting group values	Overall Study	Total	
Number of subjects	14	14	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	60.5		
standard deviation	± 14.1	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	3	3	
Race Units: Subjects			
White	10	10	
American Indian or Alaska Native	2	2	
Black or African American	2	2	

End points

End points reporting groups

Reporting group title	SNF472

Reporting group description:

SNF472 30mg/ml or 90 mg/ml solution for infusion

Subject analysis set title	Intention to Treat
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The primary analysis population for efficacy analyses was the Intention-to-Treat Population (ITT), which included subjects who received at least 1 dose of SNF472 and had at least 1 postbaseline efficacy measurement

Primary: Wound Healing

End point title	Wound Healing[1]

End point description:

The BWAT is a standardized tool for quantitative assessment of wound healing that includes the 13 items (size, depth, edges, undermining, necrotic tissue type and amount, exudate type and amount, surrounding skin color, peripheral tissue edema and induration, granulation tissue and epithelialization. Each item is rated on a scale of 1 (best) to 5 (worst). The BWAT total is the sum of the individual items with a possible range of 13 (best) to 65 (worst).

End point type	Primary

End point timeframe:

Absolute change in Bates-Jensen Wound Assessment Tool (BWAT) total score between baseline (week1) and week 12 for the primary lesion (largest lesion).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis of the primary efficacy endpoints, change in BWAT total score between baseline and Week 12 for the primary lesion was summarized descriptively and analysed using a paired Student’t t-test for the ITT population. The same analysis was conducted for the secondary efficacy endpoints of VAS and Wound Quality of Life.

End point values	SNF472			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Total Score				
arithmetic mean (standard deviation)	-8.1 (± 8.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Wound Pain

End point title	Wound Pain

End point description:

The Pain Visual Analogue Scale (VAS) is a horisontal line, 100 mm in length, anchored by word descriptors at each end. The subject marks the point on the line that represents his/her perception of his/her current pain status. The VAS was determined by measuring in millimeters from the lest hand end of the line (no pain) to the point that the subject marked. The VAS score ranges from 0 (best) to 100 (worse).

End point type	Secondary

End point timeframe:

Absolute change from baseline (week 1) to week 12 in the Pain Visual Analogue Scale (VAS) Score

End point values	SNF472			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Score				
arithmetic mean (standard deviation)	-23.6 (± 30.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Wound Quality of Life Global Score

End point title	Wound Quality of Life Global Score

End point description:

The Wound Quality of Life questionnaire measures the disease specific, health related quality of life of patients with chronic wounds. It consists of 17 items on impairments that are assessed in retrospect to the preceding 7 days and rated on a 0 (best) to 4 (worst) scale with possible responses from 'not at all' to 'very much". The total score is the average of the 17 responses.

End point type	Secondary

End point timeframe:

Absolute change from baseline (week 1) to week 12 in the Wound Quality of Life Global Score.

End point values	SNF472			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: Score				
arithmetic mean (standard deviation)	-0.9 (± 0.87)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events reported are from the time subject received the first dose of SNF472 to the last follow up visit at week 13 or early termination visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	SNF472

Reporting group description: -

Serious adverse events	SNF472		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 14 (50.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Injury, poisoning and procedural complications			
Abdominal wound dehiscence			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Dry gangrene			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive emergency			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardio-respiratory arrest			

subjects affected / exposed	1 / 14 (7.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiogenic shock				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Gastrointestinal disorders				
Haematemesis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary oedema				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Cellulitis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gangrene				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Urinary Tract Infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Fluid overload			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	SNF472		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 14 (92.86%)		
Investigations			
Electrocardiogram QT prolongation			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Haemoglobin decreased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Oxygen saturation decreased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arteriovenous fistula thrombosis			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Fall			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Laceration			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Pubis fracture			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Rib fracture			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Stress fracture			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Wound complication			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	3		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nervous system disorders			
Dyskinesia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	5		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Chest discomfort			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		

Peripheral swelling			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Dyspepsia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Rectal heamorrhage			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Skin lesion			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Skin ulcer			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Musculoskeletal and connective tissue			

disorders			
Muscle spasms			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Cellulitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperkalemia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hypernatraemia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 March 2016	Amendment 1
08 October 2016	Amendment 2
11 April 2017	Amendment 3

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study limitations included the small number of patients, lack of a control group, and open-label treatment.

Notes: